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COGNITIVE FUNCTION IN AGING COCAINE SMOKERS

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Abstract

Substance abuse disorders are becoming more prevalent in the aging population. Cocaine, specifically, is a major concern as it is the most commonly reported illegal drug associated with emergency room visits among older adults. The combined effects of aging and long-term cocaine use may significantly impact cognitive function in aging cocaine smokers; however, there is relatively little literature on this matter. The purpose of this study was to compare cognitive function in aging cocaine smokers and healthy aging individuals. The study enrolled a total of 20 participants between the ages of 50 and 60. Fourteen participants were in the aging cocaine user group and six participants were in the aging control group. Based on the separate literature on cognitive function in aging adults and chronic cocaine users, the hypothesis was that attention, working memory, and executive function in particular would be more compromised in aging cocaine smokers than in healthy aging individuals. Participants were admitted into the study for a total of five days. During this time, they underwent a series of neuropsychological assessments measuring cognitive functions such as attention, working memory, executive function, and verbal memory. Although cocaine smokers had lower scores on almost all measures, they did not perform significantly worse than healthy aging individuals on the Digit Span Forward and Backward, Trail Making Test Part A and B, and the Controlled Oral Word Association tests. The results therefore do not support our hypothesis, likely due to lack of power given the small sample size. Future studies should examine these aspects of cognitive function in larger samples of aging cocaine smokers.
Cognitive Function in Aging Cocaine Smokers

**Social History of Cocaine Smoking**

Cocaine is one of the most commonly used illegal drugs, with approximately one and a half million users in the United States alone (Substance Abuse and Mental Health Services Administration, 2010). Coca leaves were originally found thousands of years ago in the ancient Inca civilization; however, cocaine did not receive its name until German chemist Albert Neimann isolated the active ingredient in coca leaves (Gryzbowski, 2007). Initially, cocaine was used for medical purposes, as a surgical anesthetic (Gryzbowski, 2007). It was also promoted by Sigmund Freud as a treatment for depression (Levinthal, 2012). Despite these medicinal uses, it was not long before researchers learned about the negative effects of cocaine use, leading to the ban of cocaine in the US through the passing of the Harrison Narcotics Act in 1914 (Hellerman, 2011).

Several decades following the Federal Government sanction on cocaine, a resurgence of cocaine use occurred in the 1970’s when Colombian drug dealer Pablo Escobar and his cartel began trafficking cocaine into the United States (Public Broadcasting Service, 2000). By the late 1970’s, the psychoactive drug had become popular among upper-class Americans and was associated with wealthy businessmen and famous celebrities (Psychology Today, 2008). After a few years during which the cocaine industry proved to be extremely profitable, people in other regions such as the Caribbean also began producing cocaine and smuggling the drug into the United States (Osler, 2009). The proliferation of cocaine in America led to a decrease in its price and profit margins. To expand revenue, drug manufacturers experimented with cocaine and developed a new, cheaper form of cocaine known colloquially as “crack” (Osler, 2009). With the
advent of this inexpensive form of cocaine, the drug infiltrated urban areas, exacerbating the cocaine problem in America.

While “crack” and cocaine both derive from coca leaves and share the same active ingredient, there are differences between them including physical form, their administration, and the time course of their acute physical and psychological effects. Cocaine powder, formally cocaine hydrochloride, is a hydrochloride salt that comes in a white powdery form (Psychology Today, 2008). This form of the drug is ‘snorted’—inhaled through the nose—and is absorbed through the nasal tissues before entering the bloodstream three to five minutes after administration (United States Department of Justice, 1997). The high from inhaling cocaine typically lasts between 15 and 30 minutes (Foltin, Ward, Haney, Hart, & Collins, 2003).

“Crack”, or freebase cocaine, is cocaine powder that is dissolved in ammonia or baking soda to remove the hydrochloride salt (United States Department of Justice, 1997). The mixture is then boiled, producing a white (or off-white) colored rock form of cocaine (National Drug Intelligence Center, 2006). “Crack” received its street name because the rock produces a crackling sound when heated (National Institute on Drug Abuse, 2010). This form of cocaine is smoked and absorbed through the lungs rapidly, allowing the substance to enter the bloodstream and have an effect on the brain within half a minute (Strang & Edwards, 1989). The duration of the effects of smoked cocaine is only about 5 to 10 minutes, commonly leading to binge patterns of repeated self-administration (Foltin et al., 2003). Importantly, the intensity of the subjective ‘high’ achieved when cocaine is smoked is stronger than that of the drug when inhaled (Psychology Today, 2008). Volkow, Fowler, Wang, & Swanson (2008), among others, argue that the speed in which stimulants enter the brain is an important factor in the addictive potential
of that drug. This is consistent with smoked cocaine having greater abuse liability than the powder form of the drug.

Smoked cocaine was shown to have substantial abuse potential in the 1980’s when the drug became prevalent in the United States, especially in low-income urban neighborhoods (Wechsberg, Zule, Riehman, Luseno, & Lam, 2007). There were substantial negative societal effects of the increasing prevalence of cocaine smoking in these urban areas (Grogger & Willis, 1998). In order to decrease these effects, severe prison sentences were established for smoking cocaine (Public Broadcasting Service, 2000). The sentence for individuals caught with five grams of rock cocaine was a mandatory five year sentence. However, the penalties for powder cocaine use were considerably more lenient; the same five year sentence was given to individuals caught with 500 grams of powder cocaine (CNN, 2010). This 100-to-1 difference between sentences for powder and rock cocaine further impacted urban neighborhoods and led to significantly higher incarceration rates for African American cocaine users (Kerlikowske, 2013).

While the number of cocaine users has declined in the last two decades, the number of frequent cocaine users, defined as using on 51 or more days in the past year, has remained relatively stable since 1985 (Substance Abuse and Mental Health Services Administration, 2010). Adolescents and young adults who began smoking cocaine during the 1980s and 1990s who are still frequent cocaine users have sustained their drug habit for some 20 to 30 years. These individuals are now between the ages of 50 and 60 and may be facing effects of long-term cocaine smoking, as well as the normal changes associated with aging.

**Acute Subjective and Physiological Effects of Cocaine**

Cocaine, whether in powder or rock form, creates a subjective ‘high’ by stimulating the central nervous system and increasing extracellular dopamine levels—the neurotransmitter
involved in, among other functions, reward-related processing (Adamse, Gawin, Heaton, & O’Malley, 1992). The main reinforcing effects of cocaine appear to be due to cocaine occupying the dopamine transporter, inhibiting the reuptake of dopamine into the presynaptic cell, and thereby increasing dopamine levels in the synapse. In the absence of cocaine, when dopamine is released as a signal for reward or reward associated cues, the neurotransmitter is then reabsorbed into the presynaptic neuron so that it can be reused. However, cocaine prevents the dopamine from being reabsorbed, causing a sudden increase in extracellular dopamine (National Institute on Drug Abuse, 2010). Dopamine release appears to be correlated with the euphoria and ‘high’ experienced after cocaine, further indicating the importance of dopamine neurotransmission to the acute effects of cocaine (Psychology Today, 2008). Acute subjective effects of cocaine, whether smoked or inhaled, include feelings of euphoria or a “rush”, stimulation, and pleasure. Users may also experience negative acute effects such as anxiety and feelings of paranoia (Levinthal, 2012).

Aside from these subjective effects, cocaine causes acute physical side effects such as an increase in heart rate and blood pressure, constricted blood vessels, dilated pupils, and decreased appetite (Foltin et al., 1990). As the effects of the drug wear off, users may experience irritability, restlessness, and depression, as well as craving for the drug (Foltin et al., 2003). These negative effects can, in turn, lead to further cocaine use.

Long-Term Problems Associated with Cocaine Use

There are also several adverse long-term effects associated with continued cocaine use. Users who regularly inhale cocaine may begin losing their sense of smell, have nosebleeds, and have problems swallowing (National Institute on Drug Abuse, 2010; Psychology Today, 2008). Long-term cocaine smokers may experience severe respiratory problems or lung damage.
Regardless of route of administration, cocaine users are at risk for heart attack or stroke, respiratory failure, brain seizures, and death (National Institute on Drug Abuse, 2010; Psychology Today, 2008). Prolonged abuse of smoked or power cocaine can also lead to ‘cocaine psychosis’, which involves experiencing auditory hallucinations and severe anxiety and paranoia (Levinthal, 2012).

Aging Drug Users as an Emerging Problem

While previous research has primarily focused on substance abuse problems in adolescents and young adults, it is becoming increasingly apparent that it is also important to examine the causes and consequences of drug use in aging populations (Dowling, Weiss, & Condon, 2008). According to the Substance Abuse and Mental Health Services Administration (2010), the number of older adults needing substance abuse treatment will double by the year 2020. The substantial increase in these numbers is due to continued drug use amongst people from the ‘baby boomer’ generation—individuals born between 1946 and 1964 (Dowling et al., 2008). The ‘baby boomer’ generation was the first generation of adolescents who experimented widely with a range of psychoactive drugs; today, many of these aging adults are still using or abusing drugs. Given this ongoing and often long-standing drug use, many of these individuals may need treatment for drug-related problems in subsequent years.

As the number of aging individuals with substance use disorders increases, the demand for treatment and healthcare services will also rise (Dowling et al., 2008). There is evidence that this is already occurring. Since 1995, there has been a significant growth in the number of emergency room visits for illegal drugs among individuals 55 years and older (Dowling et al., 2008). According to the Drug Abuse Warning Network (DAWN) report, cocaine was the most...
commonly reported illegal drug implicated in emergency room visits among adults aged 50 or older (Substance Abuse and Mental Health Services Administration, 2010).

Dowling et al. (2008) stated “it is possible that the aging process itself may create a distinct set of problems unique to the older substance abusers.” This may produce a need for more drug treatment resources, presenting a financial challenge for governments and the healthcare industry (Dowling et al., 2008). Therefore, it is imperative that researchers better document the effects of long-term drug use in aging individuals in order to create treatment services that are suitable for this population and that address specific issues associated with drug use in aging populations.

As noted above, cocaine was the illegal drug most commonly implicated in emergency room visits in the aging population in recent years (Substance Abuse and Mental Health Services Administration, 2010). Lowering this kind of negative impact of cocaine use among aging users may necessitate the development of targeted treatment options adapted for this specific population. However, in order to design treatment strategies suitable for aging cocaine users, more research needs to be conducted on how the aging process interacts with long-term ongoing cocaine use in terms of function across a range of domains. As outlined below, cognitive function is one specific domain in which long-term aging cocaine users may experience difficulties. Thus, this area warrants further investigation.

**Cognitive Function in Cocaine Users**

Cognitive function in cocaine users has been examined by many researchers in recent decades. Studies have shown that cocaine abuse is associated with reduced function in a number of different cognitive domains including attention, memory, language, and executive functions (Jovanovski, Erb, & Zakzanis, 2005). Although most studies have shown reduced cognitive function...
function in regular cocaine users compared to healthy controls, the specific cognitive functions assessed and the neuropsychological tests used have been inconsistent between studies, resulting in some variability in findings (Pace-Schott et al., 2005).

A recent meta-analysis conducted by Jovanovski et al. (2005) showed that attentional measures had the largest effect sizes when comparing cocaine users with healthy controls, suggesting that attention is substantially impacted in cocaine users. Lezak, Howieson, & Loring (2004) argued that “attention underlies most other cognitive functions, such as memory and problem solving.” Additionally, Van Zomeren and Brouwer (1994) argued that attention includes a variety of processes such as information processing speed, focused attention, sustained attention, and divided attention. Thus, attention plays a central role in cognition, and reduced attentional function may have a substantial impact on daily function.

Another cognitive function shown to be lowered in chronic cocaine users is working memory. Working memory is the system that can process information on-line for the task at hand (Baumans, Adam, & Seron, 2012). Jovanovski et al. (2005) found that neuropsychological tests tapping working memory such as the Digit Span Backward had large effect sizes in terms of differences between cocaine users and non-users. Although working memory is a distinct cognitive function, it also requires an intact immediate attention span (Lezak, 1995). For that reason, the large effect sizes found on working memory tasks provide more evidence that cocaine users may have reduced attention relative to controls, as well as potential specific difficulties with working memory (Jovanovski et al., 2005).

Executive function has also been investigated in many studies and some tasks have shown large effect sizes (Jovanovski et al., 2005). Although executive function has been studied extensively by researchers, the concept does not yet have universally accepted definition or ‘gold
standard’ measurement approach (Jurado & Rosselli, 2007). Originally, executive function was described as a “central executive” or the cognitive domain that deals with how behavior is expressed (Jurado & Rosselli, 2007). Executive function is often considered an ‘umbrella’ term that encompasses a variety of different cognitive functions such as problem-solving, planning, goal-setting, control of attention, verbal fluency, and cognitive flexibility (Burgess, Veitch, de lacy Costello, & Shallice, 2000; Jurado & Rosselli, 2007). Common to all of these functions is that they are higher-order cognitive capacities largely dependent on prefrontal lobe function.

Several neuropsychological assessments are used to measure attention, working memory, and executive function. The Digit Span Forward and the Trail Making Test Part A measure basic attention, while the Digit Span Backward assesses working memory (Lezak et al., 2004). The Trail Making Test Part B measures cognitive flexibility and the Controlled Oral Word Association test measures verbal fluency, both of which are considered to be processes within the domain of executive function (Lezak et al., 2004).

A number of studies have shown that cocaine users performed significantly worse than controls on the Digit Span Forward and Backward task (Cunha, Nicastri, Gomes, Moino, & Peluso, 2004; Kalapatapu et al., 2011); the Trail Making Test Part A (Kalapatapu et al., 2011); the Trail Making Test Part B (Smelson, Roy, Santana, & Engelhart, 1999; De Oliveira et al., 2009); and the Controlled Oral Word Association Test (Kelley, Yeager, Pepper, & Beversdorf, 2005), suggesting that cocaine users have lowered neurocognitive function in attention, working memory, and executive function compared to non-cocaine users.

In addition to substantial research examining cognitive function in cocaine users, there has also been neuroscience research focusing on indicators of brain function and structure in relation to cocaine use. According to Jovanovski et al. (2005), the prefrontal cortex is the brain
region that is most affected by chronic cocaine use. Within the prefrontal cortex, the anterior cingulate gyrus and the orbitofrontal cortex regions specifically are altered in long-term cocaine abusers. The anterior cingulate gyrus is associated with attentional functions (Yamasaki, LaBar, & McCarthy, 2002), while the orbitofrontal cortex is implicated in executive function (Eslinger & Damasio, 1985). Additionally, the dorsolateral prefrontal cortex, which has also been found to be affected by chronic cocaine use, is linked to working memory and cognitive flexibility performance (Klüver, Murphy, & Garavan, 2005). Thus, neuropsychological findings that attention, working memory, and executive function are reduced in cocaine users relative to controls are consistent with evidence of alterations to prefrontal cortex structure and function in long-term cocaine users (Kelley et al., 2005).

Intact cognition, including memory, attention, executive function, information processing, mental flexibility, speed of processing, and goal-setting is vital to successful daily function. Chronic cocaine users who have lowered cognitive function may have difficulties with everyday tasks such as memorizing dates or numbers, driving, planning activities, and structuring work and leisure activities. Lowered cognitive function may also negatively impact response to cognitive-behavioral therapy, which is the most commonly used and most effective treatment option for cocaine dependence (National Institute on Drug Abuse, 2010) in the absence of any FDA-approved treatment medication. Cognitive-behavioral therapy (CBT) requires intact cognitive function to be able to understand and apply its strategies; a long-term cocaine user who has decreased cognitive function may struggle to learn and generalize strategies used in CBT, which may result in treatment failure (Aharonovich, Nunes, & Hasin, 2003). Aharonovich et al. (2003) found that cocaine users with mild cognitive impairments had low retention rates in outpatient CBT treatment.
Thus, cognitive function in cocaine users is important to assess, with lowered function having several important potential clinical and daily life implications. Although substantial research has already been conducted on this question, existing research has several methodological limitations. Some of these limitations include not matching control participants for race, age, gender, socioeconomic variables, and education, factors that are all themselves associated with cognitive function (See for example Goldstein et al., 2004; Adamse et al., 1992; Smelson et al., 1999).

Furthermore, other research studies did not control for recent use of cocaine or other drugs. Not controlling for these variables makes it difficult to determine if differences between the cocaine users and control participants is due to acute drug effects, residual or ‘hangover’ effects, or longer-term effects of drug use. Additionally, a lack of control for use of drugs in addition to cocaine, such as marijuana and alcohol, themselves associated with alterations to the brain and cognition, may have also affected the findings of previous studies. Finally, few studies have controlled for factors such as lack of sleep or adequate nutrition due to recent drug use. All of these factors may have increased the likelihood of reporting lowered cognitive function in cocaine users compared to controls, when such differences may in fact be due to factors other than long-term changes associated with cocaine use.

**Cognitive Function in Aging**

Normal aging is associated with changes in biology, cognition, emotions, and social behavior (Kalapatapu et al., 2011); the brain changes both structurally and functionally with age (Drag & Bieliauskas, 2009). Structurally, the brain declines in volume rapidly with increasing age, rather than changing slowly and linearly throughout the lifespan (Raz, Lindenberger, & Rodrigue, 2005). The hippocampus also deteriorates with age, affecting memory processes (Raz,
Gunning-Dixon, Head, Dupuis, & Acker, 1998). According to Drag & Bieliauskas (2009), the area of the brain that is most affected by aging is the frontal cortex. As noted above, the frontal cortex plays a large role in cognitive functions such as attention, working memory, and executive function (Jovanovski et al., 2005; Drag & Bieliauskas, 2009), functions that have been also been found to be reduced in cocaine users.

Attention is a cognitive domain that has been shown to decline with normal aging (Drag & Bieliauskas, 2009). Specifically, studies have found that older adults have difficulty with selective and divided attention (Drag & Bieliauskas, 2009). Deficits in switching between tasks, which involves both selective and divided attention, have also been reported in aging adults (Kray & Lindenberger, 2000). Another cognitive function that declines with age is memory, which has several subcomponent processes such as semantic memory and encoding and retrieving (Drag & Bieliauskas, 2009). While semantic memory or crystallized intelligence actually increases with age, fluid intelligence processes such as working memory and information processing speed decline with age (Park et al., 2002). Although semantic memory does increase with age—storing more items—recall declines, making it difficult to retrieve the knowledge stored in the brain (Drag & Bieliauskas, 2009).

Working memory is another cognitive function that has been found to decline with age (Drag & Bieliauskas, 2009). Salthouse (1996) suggested that working memory decreases with age as a result of a slower processing of single tasks. Another study found that working memory declines with age because it ‘places greater demands on cognitive resources’, as it requires the attention, information processing, and basic storage (Sliwinski & Buschke, 1999).

Although cognitive function in the aging population has been researched extensively, literature on executive function specifically is still limited (Jurado & Rosselli, 2007). Some
researchers have suggested that deficits in executive function are correlated with a general decline in functional day-to-day living skills (Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998). Additionally, Jurado & Rosselli (2007) indicated that the various cognitive functions encompassed in executive function such as problem-solving, planning, verbal fluency, and cognitive flexibility, do not all decline simultaneously or evenly, thereby making it difficult to research how executive function as a central system declines with age.

Thus, healthy aging is associated with at least some functional decline across a range of cognitive domains. Although memory decline tends to be pronounced in older adults, attention and working memory appear also to be affected by aging. Moreover, there is evidence of aging-related alterations to prefrontal cortex strongly suggesting that executive functions more broadly may also be affected by aging.

**Cognitive Function in Aging Cocaine Users**

Although there is evidence of cognitive decline in cocaine users and in healthy aging adults, almost nothing is known about cognitive function in aging cocaine users relative to their non-cocaine using counterparts. However, as noted above, cocaine users as a group are aging. Young adults who began smoking cocaine during the 1980’s are part of the baby boomer generation. These cocaine smokers are now between the ages of 50 and 60 and may be beginning to experience a decline in their cognitive function due to increasing age (Alwin & Hofer, 2011). These individuals may also have lowered cognitive function associated with long-term cocaine use (Cunha et al., 2004). The combination of long-term cocaine use and aging may cause greater decrements in cognitive function than healthy aging alone; however, this possibility has been relatively unexplored.
Kalapatapu et al. (2011) conducted a pilot study comparing cognitive function in older and younger cocaine abusers. To date, this has been the only research study to examine the combined effects of aging and cocaine use. In this study, there were a total of 80 participants; twenty participants in each of the cocaine groups and their respective healthy control groups. Older participants performed more poorly than the younger participants on the Trail Making Test A and B and the Digit Span Backward tests (Kalapatapu et al., 2011), indicating that older participants had poorer attention, cognitive flexibility, and working memory than did younger participants. Older cocaine users performed worse than older controls on Digit Span Forward. Additionally, older cocaine users performed more poorly than younger cocaine users on the Trail Making Test A and the Digit Span Forward, suggesting that attentional difficulties in older cocaine users are more pronounced than they are in younger cocaine users.

These results provided some evidence of an interaction between aging and cocaine abuse. Further, these results are consistent with other literature on attentional difficulties in long-term cocaine users. However, in common with other research on cognitive function in cocaine users, this study had many methodological limitations, including a lack of control for recent drug use, lack of control for drug use other than cocaine, failure to control for psychiatric or physical comorbidity, and no control for how participants slept or ate in the period before cognitive testing. Thus, although this study provided an initial indication that aging cocaine users may have lowered cognitive function than their non-cocaine using peers, there remains very little known about this clinically important question.

**Present Study**

Given the near-absence of research on cognitive function in aging cocaine users, the purpose of the present study was to further investigate the combined effects of aging and long-
term cocaine smoking by assessing whether aging cocaine smokers differ in their cognitive function from healthy aging non-cocaine users. Previous research has shown that cocaine use is associated with lowering of cognitive functions such as attention, working memory, and executive function (Jovanovski et al., 2005), cognitive functions which also decline with healthy aging (Drag & Bieliauskas, 2009). Furthermore, both cocaine use and aging appear to impact prefrontal cortex function and structure, a brain region strongly implicated in attention, working memory and executive functions (Kelley et al., 2005). Thus, although we assessed a broader range of cognitive functions including premorbid intelligence and verbal memory function in this study, we hypothesized that relative to controls, cocaine users would show lowered function specifically in attention, working memory, and executive function. Because of the many methodological limitations of previous research, we aimed to stringently control for possible confounding factors by matching for age, sex, and race, taking into account use of other drugs such as marijuana and alcohol, and controlling recent drug use, sleep and nutritional intake by maintaining participants in a locked inpatient unit for four days prior to cognitive testing.
Methods

Participants

Participants were recruited for this study through advertisements in the Village Voice newspaper, AM New York newspaper, craigslist, and word of mouth. The participants in the Cocaine (COC) group had first smoked cocaine at least 20 years before participation, and had smoked cocaine at least weekly for a cumulative total of 15 years. To be included in the study, they were also required to report current cocaine smoking at least twice per week, as verified by cocaine positive urine toxicology. Participants in the Control (CONT) group included individuals with and without alcohol and marijuana use to account for the varied histories of alcohol and marijuana use in the cocaine users.

Further inclusion criteria for the COC group were: current average cocaine use of at least two days per week for at least the past six months; between the age of 50 and 60; right-handed; able to perform study procedures; verbal fluency in English; and, for women, practicing an effective form of birth control.

Inclusion criteria for the CONT group were: between the age of 50 and 60; right-handed; able to perform study procedures; verbal fluency in English; and, for women, practicing an effective form of birth control.

Exclusion criteria for the COC group were: current Substance Dependence except cocaine and cigarettes (DSM-IV criteria; American Psychiatric Association, 1994); lifetime Substance Dependence except cocaine, alcohol, marijuana, and cigarettes; lifetime or current Substance Abuse except cocaine, alcohol, marijuana and cigarettes; pregnancy or current lactation; interest in drug treatment; past year mood, anxiety, or eating disorder; lifetime neurological illness or autistic spectrum disorder; lifetime manic episode or psychotic illness;
medical history likely to affect social cognition or brain function (e.g. dementia, loss of consciousness for more than 5-10 minutes following head injury, and HIV); presence of significant medical illness (including diabetes, cardiovascular disease, hypertension of more than 140/90, clinically significant laboratory abnormalities) or treatment precluding participation; recent history of significant violent behavior; clinically significant claustrophobia; left-handed; and counter-indication for MRI (e.g. metal in body).

Exclusion criteria for the CONT group were: any past cocaine use; current substance dependence except cigarettes; lifetime Substance Dependence except cigarettes, alcohol, and marijuana; lifetime or current Substance Abuse except alcohol, marijuana, and cigarettes; pregnancy or lactation; interest in drug treatment; past year mood, anxiety, or eating disorder; lifetime neurological illness or autistic spectrum disorder; lifetime manic episode or psychotic illness; medical history likely to affect social cognition or brain function (dementia, loss of consciousness for more than 5-10 minutes following head injury, and HIV); presence of significant medical illness (including diabetes, cardiovascular disease, hypertension of more than 140/90, clinically significant laboratory abnormalities) or treatment precluding participation; current parole or probation, or recent history of significant violent behavior; clinically significant claustrophobia; left-handed; and counter-indication for MRI (e.g. metal in body).

A total of 523 people were excluded from the study after going through phone screening. Reasons for exclusion included not enough cocaine use, being outside the age range specified, left-handedness, mood, anxiety, or eating disorders in the past year, lifetime mania or psychosis, metal in the body, pregnancy or current lactation, interested in drug treatment, or significant medical illness likely to contribute to neurological dysfunction (HIV, epilepsy, autism).
48 people were excluded from the study after they came in for an initial screen and interview with a psychologist and were found not to meet inclusion criteria.

**Procedure**

After potential participants called the institution to inquire about the study, a research assistant conducted an initial phone screen. The phone screen asked questions about demographic information, educational history, current occupation, and whether the volunteer had current medical problems. Following this section, there were several questions related to the individual’s drug history, including use of drugs such as cocaine, amphetamines, hallucinogens, ecstasy, heroin, marijuana, alcohol, and nicotine. The questions covered how old the individual was when they first started using the drug, how often they use the drug, and the average amount of money spent per use. The last two sections of the phone screen included questions about the candidate’s legal and medical history.

Individuals who passed the initial phone screen were then scheduled for the first outpatient screening visit. During this appointment, candidates read the study consent forms and completed intake paperwork and mood, personality, medical, and drug questionnaires. Candidates were also given a number of physical examinations including a urine drug and pregnancy (for women) test, tuberculosis test, blood pressure test, electrocardiogram (EKG), breathalyzer, and breath carbon-monoxide test to ensure safety for admission to the General Clinical Research Unit at the New York State Psychiatric Institute. Following the paperwork and physical examinations, candidates also met with a psychologist to go through their detailed drug history.

During the second or third screening visit, participants met with a medical doctor for a medical examination and a trained clinical interviewer for a structured clinical interview for
DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 2002). Written, informed consent was also obtained after the medical examination. All participants had between 2-6 screening visits to complete the screening and orientation process. During the participants’ last appointment, they were given a list of the rules of the inpatient ward and a list of items they would be able to bring with them.

Participants were admitted into the study on either a Thursday or Friday to be released on the following Tuesday or Wednesday morning. The four day inpatient period prior to testing ensured that participants did not use drugs before testing, as well as ensuring that they received adequate rest and nutrition during that time period. During the first four days of the study, participants spent all of their time in the inpatient ward at the institution. They were not permitted to leave, receive visitors, or use their cell phones. The inpatient ward had several computers available with internet access, three payphones, two televisions, a library, an art room, and a game room with a PlayStation console and a ping pong table. Participants were given options for breakfast, lunch, and dinner, and they ate at a specific time for each meal. If they were cigarette smokers, they were also taken outside to smoke cigarettes four times during the day.

On the fifth day of the study, participants were brought to the Magnetic Resonance Imaging (MRI) room at 9 am to practice the tasks they would be completing in the functional MRI. Participants underwent structural and functional Magnetic Resonance Imaging, data from which are not being presented in this thesis. Following the MRI session, participants were taken back to the inpatient ward for lunch and were given a 90 minute break. The cognitive testing sessions began at around 12:30 pm and lasted until approximately 4:30 pm. The participants spent one further night in the inpatient ward to ensure that their performance in the cognitive
testing session was not disrupted by thoughts about discharge that evening. They were discharged the morning of their sixth day. Table 1 shows the schedule for participants from admission to release.

Table 1

Schedule for Participants

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>Remain on unit</td>
<td>Remain on unit</td>
<td>Remain on unit</td>
<td>MRI and Cognitive Testing</td>
<td>Discharge</td>
</tr>
</tbody>
</table>

Before participants were released from the study, the principal investigator of the overall study fully debriefed them about the purpose of the study. Participants were able to make a total of $545 from the study and were given their payment in cash. The doctor in charge of the study also offered drug-using participants treatment referral if they were interested. Only three participants accepted treatment referral. All procedures were approved by the New York State Psychiatric Institute (NYS PI) Institutional Review Board (IRB).

Assessments

The cognitive testing session was approximately four hours long and consisted of a variety of computer and face-to-face tasks. Computerized tasks were designed to assess specific hypotheses separate from the present study and data from these tasks were therefore not included in this thesis. The following neuropsychological measures are included in this study and have been categorized based on the cognitive function assessed:
Premorbid IQ:

- *Wide Range Achievement Test 3 (WRAT3)*: The WRAT3 has three subtests, of which the reading section was used in this study. The reading subtest assesses reading skills, which includes word recognition and pronunciation (Spreen & Strauss, 1998). The WRAT3 measures crystallized intelligence which is an estimate of premorbid IQ, as it is less vulnerable to insult than other types of intelligence such as fluid intelligence (Lezak et al., 2004). Participants must read a row of letters aloud, followed by a list of 42 words. The test is scored by counting the total number of words pronounced correctly and without hesitation. (See Appendix A for a copy of the WRAT3).

Attention:

- *Digit Span Forward*: The Digit Span test, comprised of the Digit Span Forward and Digit Span Backward, is a component of the Wechsler Adult Intelligence Scale assessment (Lezak et al., 2004). Digit Span Forward measures attention and short-term memory. Participants are read a series of digits and asked to repeat the series back immediately in the same order in which it was read. The length of the series increases as the participant correctly recalls each series. A total score of 16 can be earned on this test. (See Appendix B for a copy of the Digit Span Forward).

- *Trail Making Test (TMT) Part A*: The TMT Part A is a timed task that requires participants to connect a series of 25 numbers in numerical order; this task measures simple attention (Spreen & Strauss, 1998). If a participant makes an error, the examiner draws a line where the error was made and asks the participant to start from the same
point again, without stopping the timing. The total score is the length of time taken for completion. (See Appendix C for a copy of the TMT Part A)

**Verbal Memory:**

- *Rey Auditory-Verbal Learning Test* (RAVLT): The RAVLT assesses verbal learning and memory (Lezak et al., 2004). Participants hear a list of 15 words (List A) with a 1-second interval between words. Participants are asked to recall as many words as they can remember after hearing the words in whatever order they can remember them. There are a total of five trials; the first trial measures immediate memory span, while the four subsequent trials provide a measure of verbal learning. After the fifth trial, examiners read a new list of 15 words (List B) and participants are asked to recall as many words as they can remember from this new list. The List B trial is used to measure proactive interference. Following the List B trial, participants are asked to recall words from List A again, measuring immediate recall and retroactive interference. After a 20 minute delay, participants are asked to recall words from list A, which measures delayed free recall. The RAVLT is completed with a recognition test, in which participants are asked to identify words from List A from a sheet containing all List A words, as well as List B words and several distracters. The score for each trial is the total number of words recalled correctly. (See Appendix D for a copy of the RAVLT).

**Working Memory:**

- *Digit Span Backward* measures working memory (Lezak et al., 2004). The procedure for the Digit Span Backward is similar to the Digit Span Forward, except participants are asked to recall the digits in reverse order (e.g., 9, 3, 4- participants would have to recall 4,
3, 9). The maximum score for this task is 14. (See Appendix A for a copy of the Digit Span Backward).

Executive Function:

- **Trail Making Test Part B**: The TMT Part B measures cognitive flexibility (Lezak et al., 2004). This timed task requires participants to connect a series of numbers and letters in order, alternating between numbers and letters (Lezak et al., 2004). If a participant makes an error, the examiner draws a line where the error was made and asks the participant to start from the same point again, without stopping the timing. The total score is the length of time taken for completion. (See Appendix E for a copy of the TMT Part B).

- **Controlled Oral Word Association Test** (COWAT): The COWAT measures verbal fluency; the FAS set specifically assesses phonemic fluency, while the category set (animals in this present study) assesses semantic fluency (Spreen & Strauss, 1998). Participants are given one minute each to think of as many words as they can that start with ‘F’, ‘A’, and ‘S’ respectively. Proper names cannot be used (i.e., *Boston, Bob, or Buick*) nor can the same word with a different ending (i.e., *eat and eating*). Similarly, for the category test, participants are given one minute to name as many animals as they can recall. The number of words recalled correctly is the score for each section. The number of errors can be employed as a measure of inhibition. (See Appendix F for a copy of the COWAT).

**Statistical Analysis**

The analysis for this study was completed using SPSS version 19 (SPSS Inc., Chicago, IL). Basic demographic information (age, gender, race, and education level) and substance use
habits were assessed and compared between groups using between-subjects t-tests and chi-square tests of independence. T-tests were conducted to compare group means on the WRAT3, Digit Span Forward and Backward, RAVLT, TMT Part A and B, and the COWAT\(^1\). Chi-square tests were used to compare demographic information and substance use habits. An alpha level of .05 was used for all statistical tests.

Prior to conducting t-tests, data from the cognitive testing sessions was assessed for univariate outliers, using the criteria \( z = +/- 3.29 \). There were no outliers in the data. Additionally, cognitive variables were assessed for normality of distribution; no substantive departures from normality were observed. Lastly, homogeneity of variance was assessed with Levene’s Test for Equality of Variance. Corrected degrees of freedom were employed in the case that Levene’s test indicated significant departure from homogeneity.

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\(^1\) The neuropsychological assessments used in this study measured cognitive domains that were related and not independent of each other. Multivariate analysis of variance (MANOVA) could have better addressed this issue than independent t-tests; however, we did not have an adequate sample size to employ this approach. If significant results were found, we planned to employ Bonferroni corrections of the alpha level to address the issue of inflated Type I error due to multiple tests.
Results

There were a total of 20 participants in this study; 14 were cocaine smokers (COC) and 6 were controls (CONT). All participants were African Americans from the New York City area and surrounds. In the COC group, 11 were male and 3 were female. In the CONT group, 4 were male and 2 female. Participants were between the ages of 50 and 60 with varied educational backgrounds. Table 2 presents the demographics variables for both groups. There were no significant differences in demographics characteristics between the groups.

Table 2

*Demographic Variables for COC and CONT group*

<table>
<thead>
<tr>
<th>Variable</th>
<th>COC Number (%)</th>
<th>CONT Number (%)</th>
<th>Chi-squared (df = 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>11 (78.6%)</td>
<td>4 (66.6%)</td>
<td>0.32, N.S.</td>
</tr>
<tr>
<td>African American</td>
<td>14 (100%)</td>
<td>6 (100%)</td>
<td>0.0, N.S.</td>
</tr>
<tr>
<td>Mean (S.D)</td>
<td></td>
<td></td>
<td>t(df = 18)</td>
</tr>
<tr>
<td>Age</td>
<td>51.9 (1.9)</td>
<td>52.2 (3.1)</td>
<td>t(18) = 0.21, N.S.</td>
</tr>
<tr>
<td>Education (years completed)</td>
<td>13.3 (1.9)</td>
<td>13.3 (1.5)</td>
<td>t(18) = 0.06, N.S.</td>
</tr>
</tbody>
</table>

*Note: SD = Standard Deviation. NS = not significantly different*
Table 3 presents participants’ substance use habits. Participants in the CONT group included individuals with and without alcohol and marijuana use to account for the varied histories of alcohol and marijuana use in the cocaine users. Current demographic data shows COC participants smoked cocaine an average of 4.0 (SD = 1.4) times per week and spent an average of $236.25 (SD = 150.90) per week on cocaine. All COC participants smoked cocaine as their primary route of administration.

During the screening process, participants were asked questions about other drugs including MDMA, bath salts, amphetamines or methamphetamines, hallucinogens, sedatives or downers, and PCP. Participants from the COC group did not have prior experience with these drugs or had tried them less than three times in their lives. Participants from the CONT group had no prior experience with illegal substances other than marijuana.

There were differences between the COC and CONT groups in terms of alcohol and marijuana use in the past month and in total years of alcohol and marijuana use. Eleven of the participants in the COC group had drunk alcohol in the past month, whereas none of the participants in the CONT group had drunk alcohol in the past month. Five of the participants in the COC group had smoked marijuana in the past month, whereas none of the participants in the CONT group had smoked marijuana in the past month. The average total years of alcohol use was 17.3 in the COC group and 3.1 in the CONT group. The average total years of marijuana use was 9.2 in the COC group and 3.3 in the CONT group.
Table 3

Substance Use

<table>
<thead>
<tr>
<th>Substance Use</th>
<th>COC Number (%)</th>
<th>CONT Number (%)</th>
<th>Chi-squared (df = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants Who Have Smoked Marijuana</td>
<td>13 (93%)</td>
<td>2 (33%)</td>
<td>0.54, N.S.</td>
</tr>
<tr>
<td>Participants Who Drank Alcohol Regularly (&gt;1/week)</td>
<td>11 (97%)</td>
<td>2 (33%)</td>
<td>3.9, N.S.</td>
</tr>
<tr>
<td>Cocaine Use in Past Month (per week)</td>
<td>4 (1.4)</td>
<td>0</td>
<td>t(18) = 6.92*</td>
</tr>
<tr>
<td>Money Spent on Cocaine (per week)</td>
<td>$236.50 ($150.96)</td>
<td>0</td>
<td>t(18) = 3.78*</td>
</tr>
<tr>
<td>Total Years of Regular Cocaine Use (1 &gt; week)</td>
<td>20.8 (3.9)</td>
<td>0</td>
<td>t(18) = 12.78*</td>
</tr>
<tr>
<td>Marijuana Use in Past Month (per week)</td>
<td>0.3 (0.7)</td>
<td>0</td>
<td>t(18) = 1.06, N.S.</td>
</tr>
<tr>
<td>Total Years of Regular Marijuana Use (1 &gt; week)</td>
<td>9.2 (11.7)</td>
<td>3.3 (8)</td>
<td>t(18) = 1.13, N.S.</td>
</tr>
<tr>
<td>Alcohol Use in Past Month (per week)</td>
<td>2 (2)</td>
<td>0</td>
<td>t(18) = 2.77*</td>
</tr>
<tr>
<td>Number of Alcohol Servings in Past Month (per occasion)</td>
<td>2.9 (2.6)</td>
<td>0</td>
<td>t(18) = 2.64*</td>
</tr>
<tr>
<td>Total Years of Regular Alcohol Use (1 &gt; week)</td>
<td>20.2 (16.8)</td>
<td>3.1 (7.1)</td>
<td>t(18) = 2.36*</td>
</tr>
<tr>
<td>Number of Cigarettes (daily)</td>
<td>5.6 (6.4)</td>
<td>1.7 (4.1)</td>
<td>t(18) = 1.37, N.S.</td>
</tr>
<tr>
<td>Total Years of Cigarette Use (daily use)</td>
<td>21.7 (14.1)</td>
<td>5.8 (13.2)</td>
<td>t(18) = 2.35*</td>
</tr>
</tbody>
</table>

Note: SD = Standard Deviation. NS = not significantly different. Asterisk = significance.
Cognitive Function

Table 4 presents means and standard deviations for the neuropsychological assessments except the RAVLT, which is presented in Figure 1, for the COC and CONT groups.

Premorbid IQ:
WRAT 3

The results from the independent *t*-test indicated that there was no significant difference in the number of words read correctly in the WRAT 3, *t*(18) = 0.15, *p* = 0.88.

Attention:
Digit Span Forward

There was no significant difference between groups in the number of words recalled correctly in the Digit Span Forward, *t*(18) = 0.89, *p* = 0.39.

TMT Part A

There was no significant difference in the time taken to complete the TMT A, *t*(18) = 1.19, *p* = 0.25.

Working Memory
Digit Span Backward

There was no significant difference between the groups in the score for Digits Span Backward, *t*(18) = 0.32, *p* = 0.76.

Executive Function
TMT Part B

There was no significant difference between groups in the time taken to complete this task, *t*(18) = 1.04, *p* = 0.31.

COWAT- FAS

There was no significant difference between groups in the number of words generated in the phonetic fluency component of the COWAT, *t*(18) = 1.4, *p* = 0.18.
COWAT- Animals

There was no significant difference in the number of words recalled,

\[ t(18) = 0.15, p = 0.88. \]

COWAT- Total Number of Errors in FAS and Animal Trials

There was no significant difference between groups in the number of errors made on the COWAT, \( t(18) = 0.55, p = 0.59. \)

Table 4

*Neuropsychological Assessment Scores*

<table>
<thead>
<tr>
<th>Neuropsychological Test</th>
<th>COC Mean (SD)</th>
<th>CONT Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WRAT 3</td>
<td>28.4 (2.7)</td>
<td>28.7 (4.5)</td>
</tr>
<tr>
<td>Digit Span Forward</td>
<td>9.2 (2.3)</td>
<td>10.2 (1.9)</td>
</tr>
<tr>
<td>TMT Part A</td>
<td>34.1 seconds (9.1)</td>
<td>42.3 seconds (22.7)</td>
</tr>
<tr>
<td>Digit Span Backward</td>
<td>5.1 (2.4)</td>
<td>5.5 (2.1)</td>
</tr>
<tr>
<td>TMT Part B</td>
<td>110 seconds (40.1)</td>
<td>90.8 seconds (31.2)</td>
</tr>
<tr>
<td>COWAT FAS</td>
<td>36.8 (9.1)</td>
<td>30.8 (7.4)</td>
</tr>
<tr>
<td>COWAT Animals</td>
<td>18.1 (3.9)</td>
<td>18.5 (6.6)</td>
</tr>
<tr>
<td>COWAT Total # of Errors (in FAS and Animal trials)</td>
<td>4.6 (3.1)</td>
<td>3.7 (4.8)</td>
</tr>
</tbody>
</table>

*Note: SD = Standard Deviation*
Memory
RAVLT: Trials 1-7

A t-test was conducted for RAVLT trials 1-5, immediate recall, listed as trial 6, and delayed recall, listed as trial 7. Figure 1 presents the mean number of words recalled for trials 1-7 for the COC and CONT groups. Although the cocaine smokers performed at lower levels than the controls across all trials, there were no significant differences in the number of words recalled for any of the trials.

RAVLT: Trials B

There was no significant difference in the number of words recalled for trial B, 
\[ t(18) = 0.76, p = 0.46. \]

RAVLT: Recognition

There was no significant difference in the number of words recognized in the RAVLT recognition trial, 
\[ t(18) = 1.48, p = 0.16. \]

*Figure 1:* Number of words recalled for COC and CONT groups (data are means +/- SEM)
Table 5

**Neuropsychological Assessment Scores Compared to Norms**

<table>
<thead>
<tr>
<th>Neuropsychological Tests</th>
<th>COC Mean (SD)</th>
<th>CONT Mean (SD)</th>
<th>NORMS Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit Span Forward</td>
<td>9.2 (2.3)</td>
<td>10.2 (1.9)</td>
<td>6.5 (1.1)</td>
</tr>
<tr>
<td>Digit Span Backward</td>
<td>5.1 (2.4)</td>
<td>5.5 (2.1)</td>
<td>4.7 (1.3)</td>
</tr>
<tr>
<td>TMT Part A</td>
<td>34.1 seconds (9.1)</td>
<td>42.3 seconds (22.7)</td>
<td>37.7 seconds (19)</td>
</tr>
<tr>
<td>TMT Part B</td>
<td>110 seconds (40.1)</td>
<td>90.8 seconds (31.2)</td>
<td>96 seconds (39.3)</td>
</tr>
<tr>
<td>TMT Part B-A</td>
<td>75.9 seconds (38.5)</td>
<td>48.5 seconds (28.3)</td>
<td>58.3 seconds</td>
</tr>
<tr>
<td>COWAT FAS</td>
<td>36.8 (9.1)</td>
<td>30.8 (7.4)</td>
<td>45.9 (12.3)</td>
</tr>
<tr>
<td>COWAT Category</td>
<td>18.1 (3.9)</td>
<td>18.5 (6.6)</td>
<td>23.3 (4.7)</td>
</tr>
<tr>
<td>RAVLT Trial 1</td>
<td>4.2 (1.3)</td>
<td>5.2 (1.7)</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td>RAVLT Trial 5</td>
<td>9.2 (1.9)</td>
<td>11.2 (2.3)</td>
<td>9.4 (2.7)</td>
</tr>
<tr>
<td>RAVLT Trial B</td>
<td>3.6 (1.5)</td>
<td>4.2 (1.9)</td>
<td>7 (3.4)</td>
</tr>
<tr>
<td>RAVLT Recognition</td>
<td>11.5 (2.3)</td>
<td>13 (1.7)</td>
<td>11.5 (2.7)</td>
</tr>
</tbody>
</table>

*Note: SD = Standard Deviation*

Table 5 presents the data from this study and normative data for adults between the ages of 50 and 60. All normative data was found in the *Handbook of Normative Data for Neuropsychological Assessment* (Mitrushina, Boone, & D’Elia, 1999).
Discussion

The primary objective of this study was to assess attention, working memory, and executive function in aging cocaine smokers compared to healthy aging individuals. Based on previous research, it was hypothesized that these dimensions of cognitive function would be lower in aging cocaine smokers than in healthy aging individuals. This hypothesis was not supported, with no significant differences observed between cocaine users and demographically-matched controls on any cognitive measure.

To assess attention and working memory, the following neuropsychological assessments were employed: the Digit Span Forward and the TMT Part A, which both primarily measure attention; and the Digit Span Backward, which assesses working memory. To assess executive function in both groups, two neuropsychological assessments were utilized: the TMT Part B, which measures cognitive flexibility, and the COWAT, which assesses verbal fluency and inhibition of incorrect responses. There was no statistically significant difference between groups in the scores for any of these assessments. These results differ from those of several previous studies which also examined attention, working memory, and executive function in cocaine users and in healthy aging individuals.

Several researchers have found statistically significant differences in attention between cocaine users and healthy controls. Goldstein et al. (2004) found that adult cocaine abusers performed significantly worse than healthy controls on the TMT Part A. Similar to this present study, Goldstein et al. (2004) used strict selection criteria for their study and excluded cocaine users who had a current or past dependence on other drugs. However, their study did not match control participants for basic demographic variables such as age, gender, or education level. These variables can have important effects on cognitive function.
Another study in which cocaine users performed significantly worse on the TMT Part A was conducted by Adamse et al. (1992). Their study, however, examined cognitive function in younger cocaine users (mean age was 27.7). Similar to this study, participants with a history of dependence on alcohol or drugs other than cocaine were excluded, as well as participants with any major medical, psychiatric, or learning disorders. However, control participants were only matched for age and education in this study. The significant difference between the cocaine users and healthy controls could have been because control participants were not matched for race or gender.

Cunha et al. (2004) also examined attention in cocaine users and found that cocaine users performed significantly worse on the Digit Span Forward than control participants. Comparable to this study, control participants were matched for age, gender, socioeconomic status, and education level. Additionally, Cunha et al. (2004) excluded participants who met criteria for other DSM-IV axis I disorders and any physical or mental illness. Kalapatapu et al. (2011) also found that older cocaine users performed worse than healthy control participants, as well as younger cocaine users, on the Digit Span Forward.

Compared to research on attention, there has been limited study of working memory in cocaine users. The only study in which cocaine users performed significantly worse on the Digit Span Backward was conducted by Cunha et al. (2004). As noted above, their study used demographically-matched controls and a similar research design as that used in the present study. In the pilot study examining cognitive function in aging cocaine smokers, neither older nor younger cocaine users performed significantly worse on the Digit Span Backward than their respective control groups (Kalapatapu et al., 2011).
Although other studies did not use the Digit Span Backward to examine working memory in cocaine users, other neuropsychological assessments such as the Paced Auditory Serial Addition Test and the Spatial Working Memory task have been used. Soar, Mason, Potton, & Dawkins (2012) used the Spatial Working Memory task to assess working memory and found that cocaine users performed significantly worse than healthy controls. Similar to this study, control participants were matched for age, gender, ethnicity, and education level. While their study did exclude participants with current psychiatric or physical illness, polydrug users were not excluded. In fact, the authors suggested that the participants’ high weekly alcohol consumption was a limitation of the study.

A number of researchers have found statistically significant differences in executive function between cocaine abusers and healthy controls. Smelson et al. (1999) conducted a study examining neuropsychological deficits in cocaine-dependent males and found that cocaine users performed significantly worse on the TMT Part B—a measure of cognitive flexibility—than did controls. Similarly, Rosselli, Ardila, Lubomski, Murray, and King (2001) found that cocaine users performed significantly worse on the TMT Part B. Neither study, however, matched controls to the cocaine users for age or educational level.

Verbal fluency is another component of executive function that has previously been examined in cocaine users. Kelley et al. (2005) investigated verbal fluency in relation to cocaine use and found that cocaine users performed significantly worse on the COWAT FAS and animal trials than healthy controls. In this study, healthy controls were matched for age, gender, and verbal IQ. However, Kelley et al. (2005) did not exclude participants with a history of mental illness, dependence on drugs other than alcohol and cocaine, or previous head injuries, which may have contributed to results.
Cunha et al. (2004) also found that cocaine users performed significantly worse on the COWAT than healthy controls. This study only included the FAS trials and not the animal trial. Although both Kelley et al. (2005) and Cunha et al. (2004) found verbal fluency impairments in cocaine users, other researchers have found that cocaine users did not perform worse than healthy controls on verbal fluency tasks. Surprisingly, one study even found that cocaine users performed better on the COWAT task than healthy controls (Hoff et al., 1996).

The results from this present study were also compared to normative data for adults between the ages of 50 and 60 from more diverse racial and socioeconomic backgrounds. There was no clear pattern in these findings. On some of the assessments such as the Digit Span Forward, both the COC and CONT groups performed better than the norms. Further, the COC group performed better than both the CONT group and the norms on the TMT Part A. However, on measures such as the COWAT FAS and category trials, the norms performed better than both the COC and CONT groups. Lastly, the CONT group performed better than the COC groups and the norms on a few of the assessments such as the TMT Part B and the RAVLT trial 5.

One important difference between all of the studies mentioned above and the present study is that this study required participants to stay on an inpatient ward for several days before administering the neuropsychological assessments. All of the other studies only required participants to come in for a few hours for the cognitive testing sessions. The reason participants in this study were asked to stay in the inpatient unit was to ensure they were abstinent from drugs and caffeine, were not sleep deprived, and had been eating well before participating in the neuropsychological assessments.

The secondary objective of this study was to more broadly assess cognitive function in aging cocaine users. The neuropsychological assessments used measured premorbid IQ (the
There were also no significant differences between groups in the scores for these assessments, findings that are also inconsistent with much of the existing literature.

Only one prior study also used the RAVLT to examine verbal memory. Fox, Jackson, & Sinha (2009) conducted a study on learning and memory deficits in cocaine users and found that cocaine users performed significantly worse than healthy controls on the RAVLT. Across all List A trials, cocaine users recalled significantly fewer words and made significantly more errors. Moreover, cocaine users recalled fewer words on the List B trial and the recognition test. Similar to the present study, Fox et al. (2009) control participants were matched on variables such as age, gender, and race. Additionally, participants were excluded if they met criteria for current or past dependence on drugs other than cocaine, alcohol, and nicotine. Participants with current medical problems were also excluded.

There are several possible reasons why the present results were not consistent with the hypothesis or the findings of prior studies. First, the sample size was small, with 14 participants in the cocaine-using group and 6 in the healthy control group. The small size of the control group reflects the difficulty of recruiting control participants who are well matched with cocaine users on demographic characteristics. The smaller sample size could have resulted in a larger standard error and more imprecise estimate of the effect (Hackshaw, 2008). Notably, although there were no significant differences between groups, cocaine users performed worse on almost all cognitive dimensions assessed. Therefore, these differences between the COC and CONT groups may have reached significance with a larger sample size.

Another possibility is that we did not observe differences between the groups because of the stringent control for factors that could possibly have been confounds. For instance, in
addition to the comprehensive screening process, participants were also matched for age, race, ethnicity, and education level. This is in contrast to many other studies examining cognitive function in cocaine users. Control for demographic factors such as these is important given that cognitive function decrements in cocaine users observed in previous studies may in part reflect the influence of such factors rather than cocaine use itself. Studies of cognitive function in users of other drugs have also reported that controlling for a variety of possible confounds may also reduce the effects observed, suggesting that studies failing to do so may not be reporting accurate results (Bedi & Redman, 2008). Additionally, participants in this study were asked to come to the research institute before the cognitive testing sessions, which controls for effects of lifestyle and recent drug use. Very few other studies have done that, which potentially accounts for some differences from previous studies.

**Strengths**

This study had several unique strengths. Foremost, the inclusion and exclusion criteria were strict, requiring an extensive recruitment and screening process for participants. All participants were required to undergo a structured clinical interview (SCID) to assess for any Axis I Disorders or current Substance Dependence on drugs other than cocaine, marijuana, alcohol, and cigarettes. This is important because some previous studies have not excluded for psychiatric conditions, which tend to be more prevalent in drug users and which are also themselves associated with cognitive dysfunction. Furthermore, many studies have not endeavored to address drug use other than cocaine in cocaine users, who commonly use marijuana and alcohol, both of which are also associated with lowered cognition. Participants were also required to meet with a physician for a medical examination to ascertain that they did
not have diabetes, cardiovascular disease, or any other serious medical illness, further controlling for potential confounds.

Another important strength of this study was that participants were required to stay on the inpatient ward for four days prior to the cognitive testing session, which ensured that they were abstinent from any drugs during that time. Participants who were cigarette smokers were taken outside to smoke up to four times a day; however, they were not permitted to go outside of the unit by themselves or for any other reason, or to receive visitors. The use of this controlled environment enabled us to ensure that any effects observed were not due to acute intoxication with cocaine or any other drug and was also not due to residual (“come down”) effects of drugs. This is important because studies have shown that both acute intoxication with drugs and residual effects can impact on cognitive function (Volkow et al., 2008).

The number of neuropsychological assessments used during the cognitive testing sessions is another strength of the study. While the aim of this study was to examine attention, working memory, and executive function in aging cocaine smokers, a number of other assessments were used to obtain a more comprehensive perspective on cognitive function in this population. In addition, the tests employed were clinical neuropsychological tests which are designed to detect clinically important cognitive dysfunctions, which is also a strength in terms of better understand factors that may affect treatment outcome in aging cocaine users.

Another advantage of the study is its foray into a relatively unexplored area of research. Other than the pilot study ran by Kalapatapu et al. (2011), no other study has investigated cognitive function in the aging cocaine smoking population. This study will therefore act as the basis for future research.
Limitations

The most significant limitation of this study was the small sample size. Small samples may not produce statistically significant results or precise effect sizes, particularly when the effect of interest is subtle (Hackshaw, 2008). Although the present study did not find significant differences in the scores between the COC and CONT groups, we cannot conclude that there was no difference. According to Altman & Bland (1995), the absence of a statistical significance does not imply a lack of an effect.

Another limitation of this study was the lack of diversity in race and ethnicity. All participants were African American males and females who primarily lived in the New York City area. Although this research study was not originally intended to only examine cognitive function in African Americans, individuals from other races and ethnicities were either not inquiring about the research study or were not eligible based on exclusion criteria described above.

Future Recommendations

An important future direction will be to expand this study, conducting more research examining cognitive function in the aging cocaine smoking population. Notably, almost nothing is known about cognition or other dimensions of function in this growing population of aging cocaine smokers. Although this study did not detect significant differences in cognitive function between aging cocaine smokers and healthy aging individuals, cocaine users performed worse on almost all measures of cognitive function compared to well-matched controls. Given the limited sample size, this suggests that future studies in larger samples of people may provide greater insight into cognitive function in aging cocaine users.
Another important recommendation would be for researchers who do detect significant effects to report effect sizes in their results, and whether the findings are indicative of clinically significant levels of impairment. According to Jovanovski et al. (2005), a major problem in neuropsychological research is the lack of effect sizes being reported in studies. Although the majority of researchers report statistical significant findings in their results, most have not reported the magnitude of observed effects in their results (Jovanovski et al., 2005). This lack of information in studies makes it difficult to understand how clinically significant reductions in function are in cocaine users.

Jovanovski et al. (2005) also argued that another key problem in neuropsychological research is the lack of uniformity in the neuropsychological assessments used to measure cognitive function. They go on to suggest that researchers should employ the same neuropsychological assessments in future studies. We also agree that researchers should use the same neuropsychological assessments to measure cognitive function in future studies. Comparing working memory and verbal memory results from the present study with those of other research was difficult because previous researchers had used a variety of different assessments. For example, this study and a few others used the Digit Span Backward to assess working memory, while others used assessments such as the Paced Auditory Serial Addition Test and the Spatial Working Memory task. Thus, determining whether cocaine users have working memory impairments is a challenging task due to the inconsistency in assessments used across different studies.

Prior to establishing a unified approach in neuropsychological research, there needs to be consensus as to what the best measures would be for this kind of research. Subsequently, researchers should use the same tests in future studies in order to make comparing results across
studies easier and more efficient. Having a consistent approach to conducting this research will make it easier to understand whether cocaine users are cognitively impaired and if these impairments are clinically significant.

While it is critical that future researchers use the same neuropsychological assessments, it may also be important to recruit participants from more varied racial and ethnical backgrounds. Although smoked cocaine dependence rates are reported to be higher in African Americans than other races (Chen & Kandel, 2002), the National Household Survey on Drug Abuse (2001) found that African Americans only represented 19% of those who had smoked cocaine in the last year. These data indicate that a significant portion of those who smoke cocaine are not African American. Thus, researchers should also include other racial and ethnical backgrounds to have a more representative sample of the population.

Other areas of interest for future research could be examining motor function in aging cocaine smokers. A few studies have found that cocaine users performed significantly worse than healthy controls on tasks that measured simple motor skills such as the Finger Tapping Test, Grooved Pegboard Test, and Hand Dynamometer Test (Robinson, Heaton, & O’Malley, 1999). Additionally, a number of studies have found a decrease in dopamine levels and dopamine receptor binding in aging individuals (Wong, Young, Wilson, Meltzer, & Gjedde, 1997); these changes have been associated with small changes in motor and cognitive function (Volkow et al., 1998). Thus, it would be interesting to examine the significance of dopamine reduction in aging cocaine smokers in terms of motor function.

The interaction between aging, long-term cocaine use, and psychiatric illness could also be another area of interest for future research. Several studies have found that psychiatric illnesses such as depression and schizophrenia are associated with a decrease in cognitive
performance (Baune, McAfoose, Leach, Quirk, & Mitchell, 2009; Tucker, Campion, & Silberfarb, 1975). However, there is no research on how aging, chronic drug use, and mental illness can impact cognitive function. Most studies, including this present study, excluded participants with a history of psychiatric illness in order to prevent confounding effects. Once there is more established research on the interaction between aging and long-term cocaine use, it would be interesting to investigate whether comorbidities would further decrease cognitive function in aging cocaine users.

If researchers find an interaction between aging and long-term cocaine use in future studies, it will also be important to investigate how these findings impact treatment options for this population. Previous research studies have shown that cocaine users with mild cognitive impairments had low retention rates in outpatient CBT programs (Aharonovich et al., 2003). Although outpatient CBT programs were not proven to be effective for many long-term cocaine users, inpatient CBT programs may be a possible treatment option for aging cocaine users. While an outpatient treatment program cannot ensure that individuals are abstinent from drug use, an inpatient program can implement a no drug using policy in their facility and can confirm abstinence with daily urine drug tests. Furthermore, once individuals are abstaining from drug use and are no longer experiencing symptoms of acute withdrawal, they may be able to better understand the techniques used in CBT.

Another treatment option for cocaine users who do show cognitive difficulties may be cognitive remediation therapy (CRT). CRT is a behavioral treatment approach that focuses on improving cognitive function in individuals with psychiatric illnesses or substance use disorders (Medalia, 2010). Through the use of various exercises and adaptive strategies, individuals with lowered cognitive function work on improving cognitive domains such as attention, memory,
and executive function (Medalia, 2010). Thus, CRT may be a beneficial addition to CBT for aging cocaine users if they are found to have lowered cognition, as it aims to improve cognitive function. Lastly, the use of cognitive enhancers such as amphetamine and methylphenidate, which are commonly used for ADHD, may prove to be effective in improving cognitive function in cocaine users (Brady, Johnson, Gray, & Tolliver, 2011). Although research studies have shown some indication that these medications are effective in bettering cognitive function in cocaine users, more research needs to be conducted to find the most efficacious medication for cocaine dependence.

If future research studies find that aging cocaine users have lowered cognitive function relative to healthy controls, there is a possibility that the cognitive deficits identified are premorbid rather than caused by long-term cocaine use. Studies have found that individuals with a family history of drug or alcohol dependence have eight times the risk of developing a drug addiction themselves (Merikangas et al., 1998), suggesting that there may be a genetic trait that predisposes drug use. Further, Ersche et al. (2012) compared cognitive function in stimulant-dependent individuals, their biological siblings without a history of drug use, and healthy controls, and found that executive function and response control was impaired in both drug users and their non-drug using siblings. The authors suggested that drug-dependent individuals and their siblings share a genetic trait that may be a predisposing factor for drug dependence (Ersche et al., 2012). Although this study did provide some evidence that cognitive function may be impacted by genetic traits associated with the risk of developing drug dependence, further research needs to be conducted in this area.

There is also a possibility that future studies using similar methodologies may find results consistent with this present study, indicating that cognitive function in aging cocaine smokers is
not lowered compared to healthy aging individuals. One possible reason for this may be that healthy control participants matched for demographic variables such as race, ethnicity, and socioeconomic status may have similar premorbid levels of intelligence as aging cocaine smokers, suggesting that previous findings linked cocaine use to reduced cognition were due to failure to control for important confounds. Another possible reason why cognitive function may not be lowered in this specific population is the amount of cocaine use. Participants in this study smoked cocaine an average of four times a week; this amount of cocaine use may not significantly impact cognitive function in aging users. Researchers should also investigate cognitive function in heavier cocaine smokers who meet criteria for Cocaine Abuse or Dependence.

In conclusion, we examined cognitive function in aging cocaine smokers using a number of different neuropsychological assessments. We found that the aging cocaine smokers did not perform significantly worse than healthy aging individuals on these assessments, which did not support our hypothesis that attention, working memory, and executive function is lower in aging cocaine smokers. While this study had many strengths, the primary limitation was the small sample size used. Future studies should investigate cognitive function in a much larger sample of aging cocaine users to get more generalizable results.

As the number of older adults with substance use problems continues to increase, it is imperative that further research is conducted on the interaction between aging and long-term substance use. Cocaine, specifically, demands more attention as it is the illegal drug most commonly implicated in emergency room visits in the aging population. Furthermore, aside from this present study and the pilot study conducted by Kalapatapu et al. (2011), no other research studies has examined how cognitive function is impacted by aging and long-term cocaine use.
Thus, it is crucial that more research is conducted on how long-term cocaine use impacts cognitive function, as well as other domains such as motor function and co-occurring disorders. With more substantial research conducted on aging and long-term drug use, doctors and psychologists will be able to establish better treatment programs adapted for this population.
References


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## Appendix B

### Digits Forward

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</tr>
<tr>
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<td></td>
</tr>
<tr>
<td></td>
<td>trial 2  6 - 9 - 4</td>
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<td></td>
</tr>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
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</tr>
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</tr>
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<td></td>
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</tr>
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<tr>
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<td></td>
</tr>
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### Digits Backwards

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</tr>
<tr>
<td></td>
<td>trial 2  5 - 7</td>
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</tr>
<tr>
<td>2</td>
<td>_trial 1  6 - 2 - 9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>trial 2  4 - 1 - 5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>_trial 1  3 - 2 - 7 - 9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>trial 2  4 - 9 - 6 - 8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>_trial 1  1 - 5 - 2 - 8 - 6</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td>trial 2  7 - 2 - 8 - 1 - 9 - 6 - 5 - 3</td>
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TRAIL MAKING

Part A

SAMPLE

Begin

End
Appendix D

RAVLT Sample Scoring Sheet

<table>
<thead>
<tr>
<th>Recall Trials</th>
<th>Recall Trials</th>
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<tbody>
<tr>
<td>List A A1 A2 A3 A4 A5</td>
<td>List B B1 A6 A7</td>
</tr>
<tr>
<td>drum</td>
<td>desk</td>
</tr>
<tr>
<td>curtain</td>
<td>ranger</td>
</tr>
<tr>
<td>bell</td>
<td>bird</td>
</tr>
<tr>
<td>coffee</td>
<td>shoe</td>
</tr>
<tr>
<td>school</td>
<td>stove</td>
</tr>
<tr>
<td>parent</td>
<td>mountain</td>
</tr>
<tr>
<td>moon</td>
<td>glasses</td>
</tr>
<tr>
<td>garden</td>
<td>towel</td>
</tr>
<tr>
<td>hat</td>
<td>cloud</td>
</tr>
<tr>
<td>farmer</td>
<td>boat</td>
</tr>
<tr>
<td>nose</td>
<td>lamb</td>
</tr>
<tr>
<td>turkey</td>
<td>gun</td>
</tr>
<tr>
<td>color</td>
<td>pencil</td>
</tr>
<tr>
<td>house</td>
<td>church</td>
</tr>
<tr>
<td>river</td>
<td>fish</td>
</tr>
</tbody>
</table>

# correct:

Total A1 to A5 = ____________
Trial A6 - A5 = ____________
Recognition # targets correctly identified ____________
# targets correctly identified ____________

Word List for Testing RAVLT Recognition

| bell (A) | home (SA) | towel (B) | boat (B) | glasses (B) |
| window (SA) | fish (B) | curtain (A) | hot (PA) | stocking (SB) |
| hat (A) | moon (A) | flower (SA) | parent (A) | shoe (B) |
| barn (SA) | tree (PA) | color (A) | water (SA) | teacher (SA) |
| ranger (B) | balloon (PA) | desk (B) | farmer (A) | stove (B) |
| nose (A) | bird (B) | gun (B) | rose (SPA) | nest (SPB) |
| weather (SB) | mountain (B) | crayon (SA) | cloud (B) | children (SA) |
| school (A) | coffee (A) | church (B) | house (A) | drum (A) |
| hand (PA) | mouse (PA) | turkey (A) | stranger (PB) | toffee (PA) |
| pencil (B) | river (A) | fountain (PB) | garden (A) | lamb (B) |
I am going to say a letter of the alphabet and I want you to say as quickly as you can all the words that you can think of that begin with that letter. You may say any words at all, except proper names such as the names of people or places, so you would not say "Rochester" or "Robert". Also, do not use the same word again with a different ending, such as "call" and "cating". For example, if I say "A" you could say "apple", "aunt", "acorn", or "almost". Can you think of other words beginning with the letter "A"?

(If subject says 2 appropriate words, continue with test; otherwise repeat instructions up to 2 times before discontinuing.)

That's fine. Now I'm going to give you another letter and again you say all the words beginning with that letter that you can think of. Remember, no names of people or places just ordinary words.

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<td>F/R</td>
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<td>L/W</td>
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